

### **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of Claims:**

1-25. (Canceled)

26. A method of identifying a compound that modulates the activity of an animalia tRNA splicing ligase, said method comprising:

- (a) contacting a population of 5' tRNA half molecules and a population of 3' tRNA half molecules with an animalia cell-free extract or a purified animalia tRNA splicing ligase and a compound or a member of a library of compounds; and
- (b) measuring the ligation of the half molecules, wherein a compound that modulates the activity of an animalia tRNA splicing ligase is identified if the amount of ligated half molecules in the presence of a compound is altered relative to the amount of ligated half molecules in the absence of the compound or in the presence of a negative control.

27. The method of claim 26, wherein a compound that inhibits or reduces the activity of an animalia tRNA splicing ligase is identified if the amount of ligated half molecules in the presence of a compound is decreased relative to the amount of ligated half molecules in the absence of the compound or in the presence of a negative control.

28. The method of claim 26, wherein a compound that increases or enhances the activity of an animalia tRNA splicing ligase is identified if the amount of ligated half molecules in the presence of a compound is increased relative to the amount of ligated half molecules in the absence of the compound or in the presence of a negative control.

29. The method of claim 26, wherein the termini of one of the populations of tRNA molecules is labeled with a fluorophore and the other is labeled with a quencher.

30. The method of claim 29, comprising measuring the ligation of the half molecules by measuring the fluorescence of the half molecules, wherein a compound that modulates the activity of an animalia tRNA splicing ligase is identified if the fluorescent signal in the presence of a compound is altered relative to the fluorescent signal in the absence of the compound or the presence of a negative control.

31. The method of claim 30, wherein a compound that inhibits or reduces the activity of an animalia tRNA splicing ligase is identified if the fluorescent signal in the presence of a compound is increased relative to the fluorescent signal in the absence of the compound or the presence of a negative control.

32. The method of claim 30, wherein a compound that increases or enhances the activity of an animalia tRNA splicing ligase is identified if the fluorescent signal in the presence of a compound is decreased relative to the fluorescent signal in the absence of the compound or the presence of a negative control.

33. The method of claim 26, wherein the termini of one of the populations of tRNA molecules is labeled with a fluorescent acceptor moiety and the other is labeled with a fluorescent donor moiety.

34. The method of claim 33, comprising measuring the ligation of the half molecules by measuring the fluorescence of the half molecules, wherein a compound that modulates the activity of an animalia tRNA splicing ligase is identified if the fluorescence emission of the fluorescent acceptor moiety at the wavelength of the fluorescent donor moiety in the presence of the compound is altered relative to the fluorescence emission in the absence of the compound or the presence of a negative control.

35. The method of claim 34, wherein a compound that decreases or reduces the activity of an animalia tRNA splicing ligase is identified if the fluorescence emission of the fluorescent acceptor moiety at the wavelength of the fluorescent donor moiety in the presence of the compound is decreased relative to the fluorescence emission in the absence of the compound or the presence of a negative control.

36. The method of claim 34, wherein a compound that increases or enhances the activity of an animalia tRNA splicing ligase is identified if the fluorescence emission of the fluorescent acceptor moiety at the wavelength of the fluorescent donor moiety in the presence of the compound is increased relative to the fluorescence emission in the absence of the compound or the presence of a negative control.

37. The method of claim 26, wherein the tRNA half molecules are fluorescently labeled, and wherein the ligation of the half molecules is measured by measuring the fluorescently polarized light that is emitted, wherein a compound that modulates the activity of an animalia tRNA splicing ligase is identified if the rotation of the tRNA half molecules in

the presence of the compound is altered relative to the rotation of the tRNA half molecules in the absence of the compound or the presence of a negative control.

38. The method of claim 37, wherein a compound that decreases or reduces the activity of an animalia tRNA splicing ligase is identified if the rotation of the tRNA half molecules in the presence of the compound is increased relative to the rotation of the tRNA half molecules in the absence of the compound or the presence of a negative control.

39. The method of claim 37, wherein a compound that increases or enhances the activity of an animalia tRNA splicing ligase is identified if the rotation of the tRNA half molecules in the presence of the compound is decreased relative to the rotation of the tRNA half molecules in the absence of the compound or the presence of a negative control.

40. The method of claim 26, 30, 34, or 37, wherein said cell-free extract is a mammalian cell-free extract.

41. The method of claim 40, wherein said cell-free extract is a human cell-free extract.

42. The method of claim 26, 30, 34, or 37, wherein said compound is selected from a combinatorial library of compounds comprising peptoids; random biooligomers; diversomers such as hydantoins, benzodiazepines and dipeptides; vinylogous polypeptides; nonpeptidal peptidomimetics; oligocarbamates; peptidyl phosphonates; peptide nucleic acid libraries; antibody libraries; carbohydrate libraries; and small organic molecule libraries.

43. The method of claim 42, wherein said small organic molecule libraries are libraries of benzodiazepines, isoprenoids, thiazolidinones, metathiazanones, pyrrolidines, morpholino compounds, or diazepindiones.

44. The method of claim 43, wherein said small organic molecule library is an isoprenoid library.

45. The method of claim 26, 30, 34, or 37, wherein said method further comprises a step wherein the structure of the compound that modulates tRNA splicing ligase activity is determined.

46. The method of claim 45, wherein said structure of the compound is determined by mass spectroscopy, NMR, vibrational spectroscopy, or X-ray crystallography.

47. The method of claim 26, 30, 34, or 37, further comprising a step wherein the cytotoxic activity of said compound is determined.

48. The method of claim 26, 30, 34, or 37, further comprising a step wherein the cytostatic activity of said compound is determined..